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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/913,752	11/21/2001	Darja Fercej Temeljotov	033248-017	5309

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EXAMINER	
GOLLAMUDI, SHARMILA S	

ART UNIT	PAPER NUMBER
1616	

DATE MAILED: 05/04/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/913,752	FERCEJ TEMELJOTOV ET AL.	
	Examiner	Art Unit	
	Sharmila S. Gollamudi	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 January 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16-31 and 34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-31 and 34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Receipt of Response and Amendments received on 1/21/05 is acknowledged. Claims **16-31 and 34** are pending in this application. Claims 1-15 and 32-33 stand cancelled.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The rejection of claims 16-31 and 34 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is maintained.

Response to Amendment

The amendment to claim 25 overcomes the indefiniteness of this claim. The cancellation of claims 32-33 renders the rejection under indefiniteness moot. The amendment to independent claims 16 and 27 are acknowledged, however the amendment has not overcome the rejection. The examiner notes "polysaccharides" as part of the Markush group of the hydrophilic component that is in a weight percent of 15-18. This is held to be indefinite since again the examples contain HPMC and lactose, which are both hydrophilic components and renders the component outside of applicant's claimed range. Note the prior art categorizes lactose as polysaccharide and a disaccharide polysaccharide. The examiner further notes that applicant attempts to exclude Yajima's sugar alcohols, which are defined as sugar alcohols and polysaccharides in the art. Therefore, the metes and bounds of this term is vague to one of ordinary skill in the art since applicant is using it to include certain polysaccharides and exclude others. For the purpose of examination, the examiner will utilize applicant's disclosure on page 6

of the specification to define the metes and bounds of the claims. The applicant discloses xanthan gum, acacia, and guar gum as the polysaccharide.

Further clarification is requested.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The rejection of claims 16, 24, and 29-30 under 35 U.S.C. 102(b) as being anticipated by US patent 5,707,646 to Yajima et al is maintained.

Yajima et al disclose taste masking pharmaceutical compositions in the form of tablets, capsules, dry powders, and syrup. See column 3, lines 47-50. Yajima et al teach a taste-masking polymer in a low-melting substance, which is in a concentration of 10-70%. The polymer is Eudragit E and the low-melting substance includes paraffin, wax, hydrogenated oil, palmitic acid, stearic acid, stearyl alcohol, sorbitan fatty esters, and glycerin fatty esters, etc. see column 2, line 45 to column 3, line 5. Yajima et al teach the use of excipients, binders such as hydroxypropylmethyl cellulose (HPMC), polyvinyl pyrrolidone, gelatin, ethyl cellulose, etc., lubricants, surfactants, and coating agents.

Specifically example 2 discloses 600g (19.98%) of stearyl alcohol (fatty component), 100g Eudragit, 300g (10%) clarithromycin, 100g sorbitol, 100g xylitol, 347g mannitol, 50g maltitol, and 70g (7%) magnesium oxide (adsorbant). Example 4 and 7 disclose the use of glyceryl monostearate.

Note that since the prior art teaches the instant ratio of claim 29 and the composition is not structurally different, the two compositions will behave in the same manner. If applicant asserts that the instant claims and the prior art do not behave in a similar manner, then applicant is required to structurally distinguish the claims.

Response to Amendment/Arguments

Applicant argues that the recitation "wherein the formulation is a controlled release formulation" overcomes the rejection. Applicant argues that the prior art teaches taste masking but not controlled release. Applicant argues that Yajima teaches stearyl alcohol is a hydrophilic component and it is out of the instant range. Further, applicant argues that maltitol is also a hydrophilic component. Lastly, applicant argues that Yajima discloses 10% clarithromycin is a high dosage amount.

Applicant's arguments filed 1/21/05 have been fully considered but they are not persuasive. Firstly, it should be noted that the applicant's amendments do not overcome the instant rejection. It is noted that the applicant merely recites, "controlled release" without reciting any components or specific parameters. It is the examiner's position that the prior art is in a controlled release formulation since it contains Eudragit, which is known to be a rate-controlling polymer. Therefore, since applicant has not provided any specific profile, Yajima reads on the instant invention since Yajima contains rate-controlling polymers. Further, Yajima's Eudragit is known in the art to not only taste-mask an active but it also provides controlled release. See US 5,997,905 as art of interest.

With regard to applicant's assertion that stearyl alcohol is a hydrophilic component, the examiner points out that stearyl alcohol is known in the art as a lipophilic component and thus

reads on applicant's fatty component. See US patent 4,987,271 column 6, lines 59-61 as art of interest.

With regard to Yajima's use of malitol, sucrose, etc., these are taught to be sugar alcohols and the claims only require polysaccharides to be in the amount of 5-18%. The claims have open claim language which allows for the incorporation of other hydrophilic components in any weight percent with the only restriction being that polysaccharides, alkyl-substituted cellulose ethers, adsorbants, and mixtures thereof are in the amount of 5-18%. Thus, Yajima's example 2 contains 7% magnesium oxide and reads on applicant's invention. Note also the examiner's 112, indefiniteness rejection.

Lastly, with regard to applicant's argument that Yajima contains a high dosage of clarithromycin, the examiner points out applicant is relying on a feature that is not claimed, i.e. applicant has not recited the weight percent of clarithromycin. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Accordingly, the rejection is maintained.

The rejection of claims 16, 19, 24-25, and 27-31 under 35 U.S.C. 102(b) as being anticipated by WO 95/22319 to Briskin et al is maintained.

Briskin discloses an oral composition containing 43.4% clarithromycin, 5.5% povidone, 26% carbopol, 5% hydroxypropyl cellulose (an alkyl-substituted cellulose ether), 10% glyceryl behenate, and 10% microcrystalline cellulose. See table 1 on page 8. The composition is then formulated in to a tablet or capsule. See page 7, line 7. On page 6, the method of making the

tablet is disclosed wherein the particles are sieved, dry blended and compressed to form a tablet. Briskin discloses on page 5, lines 34-35 a controlled release coating.

Note that since the prior art teaches the instant ratio of claim 29 and the composition is not structurally different, the two compositions will behave in the same manner. If applicant asserts that the instant claims and the prior art do not behave in a similar manner, then applicant is required to structurally distinguish the claims.

Response to Amendment/Arguments

Applicant argues that the recitation "wherein the formulation is a controlled release formulation" overcomes the rejection. Applicant argues that Briskin does not prepare any controlled release composition. Applicant argues that Briskin fails to disclose a final product and that Briskin discloses different active agents. Lastly, applicant argues that clarithromycin is combined with other components and glyceryl behenate is use for a different purpose, i.e. an extrusion aid.

Applicant's arguments filed 1/21/05 have been fully considered but they are not persuasive. Firstly, it should be noted that the applicant's amendments do not overcome the instant rejection. The examiner points out that example 1b utilizes carbopol, a polymer conventionally utilized in a controlled release formulation. Note US 5846983 column 5, lines 15-30 as art of interest. Moreover, Briskin discloses on page 5, lines 34-35 a controlled release coating.

Secondly, the examiner is perplexed in applicant's assertion that the prior art does not utilize the instant active agent. The examiner again points to Table 1 wherein clarithromycin is

utilized. With regard to the use of other components, the examiner points out that the instant claim language does not exclude the use of other components in the formulation.

With regard to applicant's argument that glyceryl behenate is utilized for a different purpose, the examiner points out that the applicant is claiming a product and a process of preparing the product. Thus, the prior art applied need only contain a fatty component in the instant weight percent to anticipate the instant invention.

Lastly, with regard to the process of preparing the formulation, the examiner points to page 6 wherein the general process of preparation, i.e. dry blending the components and compressing to form a tablet, is disclosed.

Accordingly, the rejection is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

1) The rejection of claims 16-18 and 24-30 under 35 U.S.C. 103(a) as being unpatentable over US patent 6,117,452 to Ahlgren et al is withdrawn.

2) The rejection of claim 22 under 35 U.S.C. 103(a) as being unpatentable over US patent 6,117,452 to Ahlgren et al in view of Gibson et al (5811120) is withdrawn.

3) The rejection of claims 17-18, 20-21, 23, and 25-28 under 35 U.S.C. 103(a) as being unpatentable over Yajima et al is maintained. The rejection of claims 21 is withdrawn.

Yajima et al disclose taste masking pharmaceutical compositions in the form of tablets, capsules, dry powders, and syrup. See column 3, lines 47-50. Yajima et al teach a taste-masking polymer in a low-melting substance, which is in a concentration of 10-70%. The polymer is Eudragit E and the low-melting substance includes paraffin, wax, hydrogenated oil, palmitic acid, stearic acid, stearyl alcohol, sorbitan fatty esters, and glycerin fatty esters, etc. see column 2, line 45 to column 3, line 5. Yajima et al teach the use of excipients, binders such as various cellulose derivatives such as hydroxypropylmethyl cellulose (HPMC), polyvinyl pyrrolidone, gelatin, ethyl cellulose, etc., lubricants, phosphates, surfactants, and coating agents. Disintegrants such as low substituted hydroxypropyl cellulose, carboxymethyl cellulose, sodium carboxymethyl cellulose, etc. see column 3, lines 60-65. Coating agents include hydroxypropylmethyl cellulose, hydroxypropyl cellulose, methylcellulose, hydroxymethylcellulose phthalate, shellac, etc. see column 4, lines 20-26.

Specifically example 2 discloses 600g (19.98%) of stearyl alcohol (fatty component), 100g Eudragit, 300g (10%) clarithromycin, 100g sorbitol, 100g xylitol, 347g mannitol, 50g maltitol, and 70g (7%) magnesium oxide (adsorbant). Also, example 6 disclose 600g (19.98%)

of stearyl alcohol (fatty component), 100g Eudragit, 300g (10%) clarithromycin, 400g (40%) sorbitol, 229g (22.9%) xylitol, 100g (10%) maltitol, 20g **(2%) magnesium oxide**, 14g (1.4%) starch, 20g **hydroxypropyl cellulose (2%)**, and 10g (1%)of sodium carboxymethyl cellulose, and 3g saccharin. Example 4 and 7 disclose the use of glyceryl monostearate. Therefore, in example 6 the weight percent of the required hydrophilic components in the Markush group is 4% and not instant 5%.

Although Yajima teaches the use of alkyl-substituted cellulose ether, the examples do not utilize the instant HPMC. Further, example 6 utilizes a weight percent of 4% of the required hydrophilic components rather than the instantly claimed lower limit of 5%. Lastly, the reference does not specify the step of compressing the mixture to form a tablet.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to look to the guidance of Yajima et al and utilize hydroxypropyl methylcellulose in place of the exemplified HPC. One would have been motivated to do so since Yajima et al teach the use of HPMC and HPC as suitable binders. Therefore, it is prima facie obvious to utilize substitute one conventional binder for another. Moreover, the manipulation of concentration of the hydrophilic components in example 6 of prior art's 4% to instant 5% is deemed to be an obvious parameter, absent a showing of criticality.

Secondly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to look to the guidance of Yajima et al and further compress the clarithromycin mixture into a tablet form. One would have been motivated to do so since Yajima et al teach the use of several forms of the oral preparation including a tablet for. Thus, the step of

compressing the mixture into a tablet form is prima facie obvious to one of ordinary skill in the art since these are conventional techniques routinely utilized in the pharmaceutical art.

Lastly, the use of additives such as surfactants, phosphates, etc, would have been obvious since Yajima teaches the use of conventional additives including surfactants and phosphates. Further, Yajima teaches several types of coating that are suitable for coating tablets, including the instant acid-resistant coatings. Therefore, depending on the intended use of the tablet, one would have been motivated to select accordingly.

Response to Arguments

Applicant argues that low substituted HPMC is not the same as HPMC with a low viscosity. Further, applicant argues that instant invention is directed to a formulation that provides a controlled release formulations requires a distinct profile and Yajima does not teach this. Lastly, applicant argues that Yajima discloses 10% clarithromycin is a high dosage amount.

Applicant's arguments filed 1/21/05 have been fully considered but they are not persuasive. Firstly, the examiner acknowledges the difference between low substituted HPMC is not the same as HPMC with a low viscosity. However, it is the examiner's position that the use of a low viscosity HPMC versus a high viscosity HPMC is obvious absent evidence of criticality since depending on the desired viscosity of the final product, one would have been motivated to select accordingly. For instance, if one wanted a low viscous product, one would utilize a low viscosity cellulose derivative and vice-versa. Therefore, absent the criticality of the viscosity, the examiner maintains her position since Yajima teaches the general concept of using the HPMC as a binder.

With regard to the applicant assertion that the instant formulation provides for a distinct release profile, the examiner points out that this "distinct profile" is not a limitation in the claims; the applicant broadly claims a "controlled release formulation". The examiner again points out that Yajima teaches Eudragit and this is a rate-controlling polymer. Regardless of Yajima's primary goal of providing taste masking, "the use of patents as references is not limited to what the patentees describe as their own invention or to the problems with which they are concerned. They are part of the literature of the art, relevant for all they contain." See *In re Heck*, 699 F.2d 1331, 1332-33, 216 USPQ 1038, 1039 (1983).

Accordingly, the rejection is maintained.

The rejection of claims 17-18, 20-23, 26, and 34 under 35 U.S.C. 103(a) as being unpatentable over WO 95/22319 to Briskin et al in view of Gibson et al (5811120) is maintained.

Briskin discloses an oral composition containing 43.4% clarithromycin, 5.5% povidone, 26% carbopol, 5% hydroxypropyl cellulose, 10% glyceryl behenate, and 10% microcrystalline cellulose. See table 1 on page 8. the composition is then formulated in to a tablet or capsule. See page 7, line 7. On page 6, the method of making the tablet is disclosed wherein the particles are sieved before compressing the tablets. A coating may be used to provide controlled release. See page 5.

Briskin et al do not specify the use of hydroxypropyl methylcellulose. Further, Briskin does not teach instant surfactant.

Gibson et al teach pharmaceutical formulations containing raloxifene. Gibson et al teaches the conventional additives in pharmaceutical formulations such as hydrophilic binders

selected from cellulose derivatives such as hydroxypropyl methylcellulose or hydroxypropyl cellulose or carboxymethyl cellulose, surfactants (sodium docosate), and lubricants (glyceryl behenate) (col. 3, line 51 to col. 4, line 26). Further, the reference teaches that the preparation of the oral formulations is well known in the art such as direct compression. The process includes mixing the active with the hydrophilic binder and surfactant, which is then, milled if necessary, drying the granules, and compressing into tablets (col. 5, lines 10-15).

It would have been obvious of one of ordinary skill in the art at the time the invention was made to combine the teachings of Briskin et al and Gibson et al and utilize the instant additives. One would have been motivated to substitute Briskin's cellulose derivative for instant cellulose derivative with the expectation of similar results since Gibson teaches that both are conventional hydrophilic binders utilized in pharmaceutical compositions and functionally equivalent. Therefore, it is prima facie obvious for one of ordinary skill to substitute functionally equivalent cellulose alkyl-substituted cellulose ether for another with the expectation of similar results since the art establishes the functional equivalency of both. Furthermore, Gibson teaches the conventional use of surfactants such as instant sodium docusate in pharmaceutical compositions. Thus, the use of conventional additives such as surfactants in the preparation of pharmaceuticals is prima facie obvious.

Response to Amendment/Arguments

Applicant argues the merits of Briskin et al and argues that Gibson does not cure the deficiencies of Briskin. Applicant does not argue the instant combination.

Applicant's arguments filed 1/21/05 have been fully considered but they are not persuasive. The merits of Briskin have been addressed above and the rejection is maintained.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharmila S. Gollamudi whose telephone number is 571-272-0614. The examiner can normally be reached on M-F (8:00-5:30), alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on 571-272-0887. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Sharmila S. Gollamudi
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